

FOOD AND DRUG ADMINISTRATION

Center for Drug Evaluation and Research

*Joint Meeting of the Advisory Committee for Reproductive Health Drugs and the
Drug Safety and Risk Management Advisory Committee*

Marriott Inn and Conference Center, University of Maryland University College (UMUC)

3501 University Blvd. East, Adelphi, Maryland

September 9, 2011

FINAL QUESTIONS TO THE COMMITTEES

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1. **DISCUSSION:** Please discuss the strength of the available evidence that suggests that the safety concerns outlined below are associated with long-term (greater than 3 to 5 years) use of bisphosphonates.

- atypical subtrochanteric and femoral fractures
- osteonecrosis of the jaw
- esophageal cancer

2. **DISCUSSION:** Please discuss whether the data presented support the effectiveness of long-term (greater than 3 to 5 years) use of bisphosphonates.

Does this apply to all patients undergoing treatment for osteoporosis or to a subset of patients, such as patients with a T-score of <-2.5 and/or a prior history of fracture?

3. **DISCUSSION:** Please discuss the overall risks and benefits of continuous long-term use (greater than 3 to 5 years) of bisphosphonates.

4. **DISCUSSION:** Please discuss whether restricting the duration of use or implementing a drug holiday would be beneficial for patients requiring long term bisphosphonate treatment for osteoporosis.

Does this apply to all patients undergoing treatment for osteoporosis or to a subset of patients, such as patients with a T-score of <-2.5 and/or a prior history of fracture?

5. **VOTE:** Bisphosphonate labeling for prevention or treatment of osteoporosis currently carries the following “Important Limitation of Use”:

The safety and effectiveness of [drug] for the treatment of osteoporosis are based on clinical data of [xx] years duration. The optimal duration of use has not been determined. All patients on bisphosphonate therapy should have the need for continued therapy re-evaluated on a periodic basis.

Do you recommend that the label should further clarify the duration of use for bisphosphonates?

- If yes, please outline your recommendation

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FINAL QUESTIONS TO THE COMMITTEES (cont.)

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6. **DISCUSSION:** Please discuss for which outcomes further evidence should be obtained, how best that might be accomplished and in what priority order they should be investigated:
- atypical subtrochanteric and femoral fractures
 - osteonecrosis of the jaw
 - esophageal cancer
 - osteoporotic fracture reduction efficacy with long-term (greater than 3-5 years) continuous bisphosphonate use
 - the effect of a drug holiday on bisphosphonate safety and effectiveness